REMARKS

Claims 1, 3, 5 – 15 and 18 are pending in the application. Claims 2, 4, 12 – 14 and 16 and 17 have been cancelled. Claims 1, 3 and 15 have been amended. No new claims have been added. No new matter has been added, support for the amendments being found throughout the specification and the claims as originally filed. Specifically, support for the amendment to claims 1, 3 and 15 can be found in the specification, for example in the second sentence of paragraph [0005].

No new matter has been added. Any cancellation of the claims should in no way be construed as acquiescence to any of the Examiner's rejections and was done solely to expedite the prosecution of the application. Applicant reserves the right to pursue the claims as originally filed in this or a separate application(s).

Claim Rejections Withdrawn

Applicants thank the Examiner for reconsideration and withdrawal of the rejection of claims 1 – 11 and 15 – 18 under 35 USC §112, first paragraph.

Applicants thank the Examiner for reconsideration and withdrawal of the rejection of claims 1 – 3, 15, 17, and 18 under 35 USC §102(b).

Applicants thank the Examiner for reconsideration and withdrawal of the rejection of claims 1 – 11 and 15 – 18 under 35 USC §102(e).

Rejection of claims 1 – 3, 15, 17 and 18 under 35 USC §103

Claims 1-3, 15, 17, and 18 were rejected under 35 USC § 103(a) as being unpatentable over Lindquist et al (US 2004/0014662; the '662 reference herein) in view of Steindler et al. (US 6,638,763; the '763 reference herein). Applicants respectfully traverse this rejection.

The instant invention is based on the discovery that LPA is useful for initiating and maintaining neural stem/progenitor cell growth and differentiation in vitro, and it is taught in

the disclosure that neural stem cells can be successfully cultured in medium containing LPA **in lieu of EGF and FGF2**. Claim 1, as amended, recites a tissue culture system that comprises (a) at least one neural stem/progenitor cell isolated from subependymal zone or hippocampus, expressing at least one LPA receptor, (b) a lysophosphatidic acid (LPA) compound selected from the group consisting of LPA 20:5, 18:1 (oleoyl), 16:0 (palmitoyl), and 14:0 (myristoyl) at a concentration range from 1 μM to 50 μM; and (c) a basal culture medium comprising insulin and methyl cellulose, but **free of EGF and FGF2**.

The '662 reference fails to teach or suggest each and every element set forth in the instant claims. Nowhere does the '662 reference teach or suggest a culture system that is free of EGF and FGF2. The '662 reference relates generally to methods of influencing adult neural stem cells and neural progenitor cells to produce progeny that can replace damaged or missing neurons or other central nervous system (CNS) cell types. The '662 reference teaches neuroshphere cultures that contain EGF. Applicants direct the examiner to paragraphs [0205] and [0206] which describes the neuroshphere medium:

> Neurosphere medium (DMEM/F12, B27 supplement, 12.5 mM HEPES pH7.4) **containing 20 ng/ml EGF** (unless otherwise stated), 100units/ml penicillin and 100 .mu.g/ml streptomycin. [0205], emphasis added.
>
> To split neurosphere cultures, neurospheres were collected by centrifugation at 160.times.g for 5 min. The neurospheres were resuspended in 0.5 ml Trypsin/EDTA in HBSS (1.times.), incubated at 37.degree. C. for 2 min and triturated gently to aid dissociation. Following a further 3 min incubation at 37.degree. C. and trituration, 3 volumes of ice cold NSPH-media-EGF were added to stop further trypsin activity. The cells were pelleted at 220.times.g for 4 min, resuspended in **fresh Neurosphere medium supplemented with 20 ng/ml EGF and 1 nM bFGF** plated out and incubated at 37.degree. C. [0206], emphasis added.

The '763 reference teaches methods for obtaining a purified population of primitive human brain stem cells. The '763 reference teaches culturing of Type II and Type II

spheres in the presence of both EGF and FGF2. Applicants direct the Examiner to Examples 2 and 3 (column 11 –12):

> Cells were plated and fed as described above for the type I cells. However, the basic media described above (comprising insulin (5 .mu.g/mL), putrescine (100 .mu.M), progesterone (20 .mu.M), sodium selenite (30 .mu.M), pituitary extract (20 .mu.g/mL),transferrin (100 .mu.g/mL), and 5% fetal calf serum (FCS) in DMEM/F12 media) **also contained 10 ng/mL basic fibroblast growth factor (bFGF), and 10 ng/mL epidermal growth factor (EGF).**

The Examiner argues that the '763 reference teaches "a culture medium for neural stem/ progenitor cells within neurospheres containing methyl cellulose and insulin" (Office Action, p.5). However, nowhere does the '763 reference teach or suggest that the neurospheres (Type II or II clones) can be cultured in the absence of EGF and FGF. Clearly, the claimed invention is not obvious in view of the cite art.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the foregoing rejection.

Conclusion

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Dated: January 3, 2008

Respectfully submitted,
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